

In the Claims

1. (Previously presented) A method to reduce induced apoptosis relative to induced apoptosis caused by presenilin 2 mediated by a protein-protein interaction between presenilin 2 and a mutated human calcium-binding protein, the method comprising:

administering an effective amount of ~~a the mutant calcium-binding protein to inhibit interaction of presenilin 2 comprising an amino acid sequence as set forth in SEQ ID NO: 1 with the mutated calcium-binding protein~~, comprising a substitution of at least one amino acid residue in at least one of the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the calcium-binding EF-hands include amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2.

2. (Original) The method according to claim 1, wherein the presenilin 2 is a human protein.
3. (Cancelled)
4. - 8. (Currently cancelled)
9. (Previously presented) The method according to claim 1, wherein at least one acidic residue in the EF-hands is substituted with its amine counterpart, wherein the acidic residue comprises aspartate or glutamate and the respective amine counterpart comprises asparagine or glutamine.
10. - 11. (Currently cancelled)
12. (Currently amended) A purified mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 2 and having a substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2, and wherein the calcium-binding EF-hands include amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2.
13. - 22. (Currently cancelled)
23. (Previously presented) An *in vitro* method of reducing apoptosis in neuronal cells relative to apoptosis caused by presenilin 2 comprising:

administering a mutated calcium-binding protein, ~~in a sufficient amount to effect protein-protein interaction between the mutated calcium-binding protein and presenilin 2~~, wherein the mutated calcium-binding protein comprises at least one substitution in the amino acid residues in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the calcium-binding EF-hands include amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2.

24. (Currently amended) An *in vitro* method to reduce induced apoptosis relative to apoptosis caused by presenilin 2 ~~mediated by protein-protein interaction between presenilin 2 and a calcium-binding protein~~, the method comprising:

administering an effective amount of the mutant calcium-binding protein ~~to reduce induced apoptosis inhibit interaction of presenilin 2 comprising the amino acid sequence as set forth in SEQ ID NO: 1 with calmyrin protein comprising the amino acid sequence as set forth in SEQ ID NO: 2~~, wherein the mutant calcium-binding protein comprises inhibiting the protein-protein interaction is effected by at least one mutation selected from the group consisting of:

- 1) ~~substituting at least one amino acid residue at position 287, 288 or 297 of SEQ ID NO: 1;~~
- 2) substituting at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, wherein the calcium-binding hands include amino acid residues at positions 116 to 128 or 161 to 173 of SEQ ID NO: 2;
- 3) ~~substituting at least one N-terminal residue at positions 2 or 3 of SEQ ID NO: 2; and~~
- 4) substituting at least one amino acid residue at position 2, 127 or 172 of SEQ ID NO: 2.

25. (Currently amended) An *in vitro* method to reduce induced apoptosis relative to apoptosis caused by ~~mediated by a protein-protein interaction between presenilin 2 and a mutated human calcium-binding protein~~, the method comprising:

contacting cells with an effective amount of the mutant calcium-binding protein ~~to inhibit interaction of presenilin 2~~ comprising an amino acid sequence as set forth in SEQ ID NO: 1 with the mutated calcium-binding protein, comprising a substitution of at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the calcium-binding hands includes amino acid residues at positions 116 to 128 and 161 to 173 of SEQ ID NO: 2.

26. (Currently cancelled)

27. (Currently amended) The purified mutant calcium-binding protein according to claim 12, wherein the substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2 comprises amino acid residues at positions 116 to 128, wherein the mutation comprises replacement of an acidic residue with its amine counterpart.
28. (Previously presented) The purified mutant calcium-binding protein according to claim 27, wherein the substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2 comprises amino acid residue at position 127.
29. (Previously presented) The purified mutant calcium-binding protein according to claim 28, further comprising a substitutions at amino acid residues 2 and 172.
30. – 32. (Currently cancelled)
33. (New) A purified mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 2 and having a substitution of at least one amino acid residue in at least one calcium-binding EF-hand of SEQ ID NO: 2, and wherein the mutation comprises replacement of an acidic residue with its amine counterpart.
34. (New) An *in vitro* method to reduce induced apoptosis relative to apoptosis caused by presenilin 2, the method comprising:
- contacting cells with an effective amount of the mutant calcium-binding protein comprising an amino acid sequence as set forth in SEQ ID NO: 1 with the mutated calcium-binding protein, wherein the mutated calcium-binding protein comprises a substitution of at least one amino acid residue in the calcium-binding EF-hands of SEQ ID NO: 2, and wherein the substitution comprises replacement of an acidic residue with its amine counterpart.
35. (New) The purified mutant calcium-binding protein according to claim 33, wherein the replacement of an acidic residue with its amine counterpart is at residue 127 or 172.